

## The Effects of Vancomycin Use and De-escalation in Patients Hospitalized with Pneumonia

Aryn S. You PharmD; Bryce T. Fukunaga PharmD; Alexandra L. Hanlon PhD; Alicia J. Lozano MS; and Roy A. Goo PharmD

HJMPH contributing editors of the Daniel K. Inouye College of Pharmacy (DKICP) Scripts column are Carolyn Ma PharmD, BCOP, and Jarred Prudencio PharmD, BCACP, BC-ADM. Dr. Ma is currently Associate Professor and Dean for the University of Hawai'i at Hilo DKICP, and is a Board Certified Oncology Pharmacy Specialist with experiences in health systems administration and pharmacy academe. Dr. Prudencio is currently Assistant Professor of Pharmacy Practice, and is a Board Certified Ambulatory Care Pharmacy Specialist with experience in outpatient family medicine and specialty clinics.

### Abstract

Methicillin-resistant *Staphylococcus aureus* (MRSA) causes about 80,000 severe infections each year. Compared to Methicillin-susceptible *Staphylococcus aureus* (MSSA), MRSA is associated with higher mortality and increased hospital length of stay (LOS). Vancomycin hydrochloride, an antibiotic with activity against MRSA is often used as empiric therapy for pneumonia. However, current pneumonia treatment guidelines recommend against the routine use of MRSA coverage since MRSA prevalence rates are low. In this retrospective, observational study, 38.3% of the population received vancomycin while only 2.6% had evidence of a MRSA infection. Data was gathered manually from electronic medical records from four hospitals over a six-month period. To identify a well-balanced comparison and account for potential confounders, matching on the propensity scores was conducted. Prior to matching, those who received vancomycin had a significantly higher rate of mortality (14.3% vs 4.9%,  $P < .001$ ) and higher LOS (9.6 days vs 7.2 days,  $P < .001$ ). Those who were de-escalated from vancomycin had a significantly lower LOS (8.3 days vs 11.6 days,  $P = .001$ ) with no difference in mortality. After performing a survival analysis on matching data, those who received vancomycin had a significantly higher LOS (9.2 days vs 7.5 days,  $P = .002$ ) with no difference in mortality ( $P = .1737$ ). Those who were de-escalated had a significantly lower LOS (8.3 days vs 11.3 days,  $P = .005$ ) with no difference in mortality ( $P = .8624$ ). This study demonstrates a low prevalence of MRSA with the potential overuse of vancomycin. This along with no difference in mortality and a lower LOS supports the recommendation to limit vancomycin use as clinically appropriate. If vancomycin is used, assessment for rapid de-escalation is needed.

### Keywords

De-escalation, length of stay, methicillin-resistant *Staphylococcus aureus*, methicillin-susceptible *Staphylococcus aureus*, mortality, pneumonia, vancomycin

### Abbreviations

ASMD: Absolute standardized mean differences  
ATS: American Thoracic Society  
CAP: community acquired pneumonia  
COPD: chronic obstructive pulmonary disease  
HAP: hospital-acquired pneumonia  
HCAP: healthcare-associated pneumonia  
HPH: Hawai'i Pacific Health  
ICU: intensive care unit  
IDSA: Infectious Disease Society of America

IQR: interquartile ranges

KM: Kaplan-Meier

LOS: length of stay

MRSA: Methicillin-resistant *Staphylococcus aureus*

MSSA: Methicillin-susceptible *Staphylococcus aureus*

PCR: polymerase chain reaction

VAP: ventilator-associated pneumonia

### Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) causes approximately 80,000 severe infections and 11,000 deaths each year.<sup>1</sup> These infections can range from skin and soft tissue infections to pneumonia and bacteremia and are associated with higher mortality and increased hospital length of stay (LOS) when compared to methicillin-susceptible *Staphylococcus aureus* (MSSA) infections. Due to the high mortality rates associated with MRSA infections, clinicians often empirically treat patients with vancomycin. Vancomycin is an antibiotic with activity against MRSA and is one of the most commonly prescribed inpatient antibiotics.<sup>2</sup> Current treatment guidelines [2016 Hospital-Acquired (HAP) and Ventilator-Associated Pneumonia (VAP) and 2007 Community-Acquired Pneumonia (CAP)] from the Infectious Disease Society of America (IDSA) and American Thoracic Society (ATS) do not recommend routine use of MRSA coverage.<sup>3,4</sup> The estimated prevalence of MRSA in pneumonia is 1% to 5% for CAP and 20% to 40% in HAP.<sup>5-8</sup> In Hawai'i, the 2015 MRSA prevalence was 38.2%.<sup>9</sup> These estimates demonstrate that empiric treatment with vancomycin, which initially may have been appropriate, is theoretically not needed in most patients. In these patients, the use of an "unnecessary" antibiotic could lead to antibiotic resistance.<sup>1</sup> The Centers for Disease Control and Prevention (CDC) states that up to 50% of antibiotics are inappropriately prescribed.<sup>1</sup> One of the tools that can be used to help prevent antibiotic resistance is antibiotic de-escalation where initial empiric "broad" antibiotics, which cover many types of bacteria, can be switched to a "narrow" antibiotic that covers only a few types of bacteria once cultures and sensitivities return. Ideally, antibiotics should be de-escalated to target the pathogen of interest. In the case with

pneumonia, since MRSA rates are low, de-escalation can help to reduce the unnecessary use of vancomycin.

A study by Schlueter M., et al, found that in culture-negative healthcare-associated pneumonia (HCAP), de-escalation was associated with significantly lower inpatient mortality, significantly shorter hospital LOS, and significantly lower costs.<sup>10</sup> These benefits show the need for de-escalation interventions in pneumonia. Additionally, there are studies showing higher efficacy of beta-lactam antibiotics over vancomycin for the treatment of MRSA negative infections demonstrating effective treatment without the use of vancomycin.<sup>11-13</sup> The IDSA recommends de-escalation from vancomycin if there is no growth on cultures for 48 hours, no evidence of MRSA growth on cultures, or if a MRSA nasal polymerase chain reaction (PCR) is negative.<sup>2</sup>

MRSA nasal PCR tests for the presence of MRSA colonization in the nares. There have been studies correlating the presence of MRSA nasal colonization and culture-positive MRSA pneumonia infections.<sup>13,14</sup> MRSA nasal PCRs appear to have a high negative predictive value, up to 99.2%.<sup>14,15</sup> This suggests that if the PCR is negative, the patient is likely not colonized with MRSA in the nares and they have a very low incidence of having MRSA in the lungs. Another benefit of MRSA PCRs is that results can return within 24 hours which provides a quick and useful tool for de-escalation even before culture results are finalized.<sup>14,15</sup>

The low prevalence of MRSA pneumonia along with the potential overuse of vancomycin creates opportunities for de-escalation and the prevention of unnecessary antibiotic use. More studies on the relationship between vancomycin use in pneumonia and vancomycin de-escalation in pneumonia are needed. The purpose of this study was to determine the effects of using vancomycin in the treatment of pneumonia and to determine the effects of de-escalating vancomycin in the treatment of pneumonia.

## Methods

### Study Design and Patients

This was an exempt, retrospective chart review study (University of Hawai'i Institutional Review Board) of patients patients at least 18 years of age or older with a primary or secondary diagnosis of pneumonia who received at least one antibiotic during hospitalization. This study consisted of two comparisons with a total of four groups. The first comparison (vancomycin comparison) compared patients with pneumonia who received vancomycin compared to patients with pneumonia who did not receive vancomycin during their hospitalization. The second comparison (de-escalation comparison) involved only patients with pneumonia who received vancomycin. In this comparison, patients who were de-escalated (vancomycin duration of  $\leq 3$  days) from vancomycin during their hospitalization were compared to those who were not de-escalated (vancomycin duration  $> 3$  days). A list of patients was generated in September 2016 based on a diagnosis of pneumonia during hospitalization. Study patients had admission dates from March 2016 to August 2016 from the four hospitals that comprise the Hawai'i Pacific

Health (HPH) Systems: Kapiolani Medical Center for Women and Children (Honolulu, Hawai'i), Straub Medical Center (Honolulu, Hawai'i), Pali Momi Medical Center (Aiea, Hawai'i), and Wilcox Memorial Hospital (Lihue, Hawai'i). Patients were excluded if they were pregnant, had a concurrent documented or suspected infection requiring antibiotic therapy, or had a hypersensitivity to vancomycin. In the de-escalation subgroup analysis, patients were excluded if they did not receive vancomycin during their hospitalization, if there were any positive MRSA findings (blood or sputum culture positive for MRSA or a positive MRSA nasal PCR), or if they had a hospital LOS of  $\leq 3$  days or died  $\leq 3$  days from the date of admission.

Baseline data was gathered on age, gender (female/male), intensive care unit (ICU) admission, sepsis, prior antibiotic use in the past 90 days of hospital admission, any MRSA positive cultures, and comorbidities such as diabetes mellitus, chronic obstructive pulmonary disease (COPD), renal disease, and immunocompromised status.

### Outcomes

For both comparisons, the primary outcomes were death and hospital LOS. Mortality was defined as death from any cause during hospitalization. LOS was defined as the number of days hospitalized.

### Statistical Analysis

Descriptive statistics were generated to characterize the sample. Means, standard deviations, medians and interquartile ranges (IQRs) were used to describe continuous variables. Frequencies and percentages were used to describe dichotomous variables. Chi-square or Fisher's exact tests were used to examine differences in baseline characteristics for patients with pneumonia who received vancomycin during their hospitalization versus those who did not. Two-sample t-tests were used to compare normally distributed continuous variables, such as age, across the two groups, while non-parametric Kruskal-Wallis tests were used for comparisons of non-normally distributed continuous variables. Differences in baseline characteristics for the subgroup of patients with pneumonia who received vancomycin that were de-escalated versus not de-escalated were also examined.

Separate propensity score models were used to match patients with pneumonia in the vancomycin comparison groups as well as the de-escalation comparison groups to account for the covariates. Logistic regression models were used to estimate a propensity score using variables known to be associated with receiving vancomycin (or de-escalation from vancomycin) and each outcome of interest (mortality, hospital LOS). These variables included: age, gender, diabetes, COPD, immunocompromised status, renal disease, sepsis, prior antibiotics within 90 days, ICU admission, and positive MRSA findings. Note that positive MRSA findings were not included as a matching variable for de-escalation groups. The propensity scores from each respective logistic regression model were used to match patients with the closest propensity score on a ratio of 1:1 using a nearest neighbor approach with no replacements and specifying a caliper of 0.25. Absolute standardized mean differences

(ASMDs) were used as a balance statistic for individual covariates for each model, where an ASMD below 0.20 is desirable for all variables.<sup>16</sup>

Overall survival was estimated in the unmatched and matched samples using Kaplan-Meier (KM) methodology with comparisons accomplished using log-rank statistics. Additionally, separate backwards selection Poisson regression models were used to examine predictors of patients' LOS in the unmatched samples. Potential predictor variables considered for inclusion were: vancomycin (or de-escalation) group, age, sex, diabetes, COPD, immunocompromised status, renal disease, sepsis, prior antibiotic use within 90 days, and ICU admission. Differences in expected LOS between the matched vancomycin groups and the matched de-escalation groups were estimated using simple Poisson regression models, where hospital LOS in days was regressed on the group variable. To account for multiplicity, statistical significance was considered at the  $0.05/2=0.025$  level.<sup>17</sup> Propensity score matching procedures were conducted using the *MatchIt* package in R, which required no missing values in the data before matching.<sup>18</sup> With the exception of immunocompromised status (n=1), no missing values were observed for all matching variables. To deal with the missing value for immunocompromised status, the mode was used to replace this entry prior to matching.<sup>19</sup> All other analyses were conducted using SAS software, version 9.4 (SAS Institute Inc., Cary, NC).

## Results

### Vancomycin Comparison

Of the total 946 patients with available data, 178 were excluded, with 162 being due to concurrent infection. Nine were excluded for having no antibiotics used during hospitalization, 4 patients were pregnant, 2 patients had duplicate entries on the data list, and 1 electronic medical record could not be found. The remaining sample of 768 patients was diagnosed with pneumonia, with 294 patients (38.3%) having received vancomycin and 474 patients (61.7%) who did not. Baseline characteristics of all patients by group before and after matching are listed in Table 1. Several significant differences in baseline characteristics were found between patients that received vancomycin versus those who did not prior to matching. Specifically, patients who received vancomycin were significantly younger (mean=67.0 vs 71.0,  $P=.001$ ), more likely to have renal disease (32.0% vs 22.2%,  $P=.003$ ) and sepsis (47.6% vs 25.1%,  $P<.001$ ), more likely to be admitted to the ICU (34.7% vs 17.5%,  $P<.001$ ), and more likely to have received prior antibiotics within the last 90 days (33.0% vs 23.0%,  $P=.002$ ) compared to those who did not receive vancomycin. Among the 768 patients who were diagnosed with pneumonia, a total of 20 patients (2.6%) had an MRSA positive culture. The remaining 748 patients (97.4%) either did not have cultures collected or had cultures that did not grow MRSA.

Variable	Unmatched Sample (N=768)			Matched Sample (N=514)		
	No vancomycin (n=474)	Vancomycin (n=294)	P value	No vancomycin (n=257)	Vancomycin (n=257)	P value
<b>Baseline Characteristics</b>						
Age (years), mean (SD) median (IQR)	71.0 (16.5) 73 (62, 84)	67.0 (16.7) 67 (58, 80)	.001*	67.9 (17.5) 69 (58, 82)	67.9 (16.4) 67 (59, 80)	.96
Male, n (%)	272 (57.4%)	172 (58.5%)	.76	147 (57.2%)	147 (57.2%)	>.99
Diabetes, n (%)	164 (34.6%)	107 (36.4%)	.61	91 (35.4%)	95 (37.0%)	.71
COPD, n (%)	120 (25.3%)	69 (23.5%)	.56	55 (21.4%)	58 (22.6%)	.75
Immunocompromised, n (%)	30 (6.3%)	29 (9.9%)	.075	26 (10.1%)	26 (10.1%)	>.99
Renal disease, n (%)	105 (22.2%)	94 (32.0%)	.003*	74 (28.8%)	77 (30.0%)	.77
Sepsis, n (%)	119 (25.1%)	140 (47.6%)	<.001*	97 (37.7%)	106 (41.2%)	.42
ICU admission, n (%)	83 (17.5%)	102 (34.7%)	<.001*	67 (26.1%)	78 (30.4%)	.28
Prior antibiotics within 90 days, n (%)	109 (23.0%)	97 (33.0%)	.002*	78 (30.4%)	76 (29.6%)	.85
MRSA positive, n (%)	5 (1.1%)	15 (5.1%)	.001*	5 (1.9%)	10 (3.9%)	.190
Antibiotic therapy treatment duration** (days), mean (SD) median (IQR)	5.8 (4.4) 5 (3, 7)	7.9 (5.4) 7 (4, 10)	<.001*	5.9 (4.0) 5 (3, 7)	7.7 (5.2) 6 (4, 9)	<.001*
Number of antibiotics**, mean (SD) median (IQR)	2.4 (1.0) 2 (2, 3)	2.9 (1.3) 3 (2, 4)	<.001*	2.4 (1.1) 2 (2, 3)	2.9 (1.3) 3 (2, 4)	<.001*
<b>Primary Outcomes</b>						
Mortality, n (%)	23 (4.9%)	42 (14.3%)	<.001*	17 (6.6%)	32 (12.5%)	.024*
Hospital length of stay (days), mean (SD) median (IQR)	7.2 (4.7) 6 (4, 9)	9.6 (7.1) 8 (5, 12)	<.001*	7.5 (4.9) 6 (4, 9)	9.2 (6.7) 7 (5, 11)	.002*

\* $P < .025$ ; \*\*Not included as a matching variable in propensity score modeling.

Propensity score matching narrowed the total sample size from 768 to an equally matched sample of 514 patients (257 in each group). In the matched samples, all ASMDs were below 0.20, indicating patients who received vancomycin and those who did not were well-matched on all baseline characteristics. No significant differences in baseline characteristics were found between the vancomycin groups after matching (Table 1). There were statistically significant differences in mortality between the vancomycin groups prior to matching (log-rank  $P=0.008$ ). There was a statistically significant difference in the distribution of mortality between the groups after matching (Table 1, 6.6% vs 12.5%,  $P=0.024$ ) with more deaths in those who received vancomycin. However, the Kaplan-Meier method found no significant differences in mortality after matching on baseline characteristics (Figure 1, log-rank  $P=0.174$ ).

Prior to matching, median hospital LOS in days among patients who received vancomycin was 8 days (IQR=5, 12) compared to 6 days (IQR=4, 9) in those who did not receive vancomycin (Table 1,  $P<0.001$ ). Results from a backwards selection Poisson regression model demonstrated that patients' hospital LOS was significantly associated with the vancomycin group ( $P<0.001$ ), sepsis ( $P=0.010$ ), ICU admission ( $P<0.001$ ), and age ( $P<0.001$ ) in the unmatched sample. Specifically, the expected hospital LOS in days among patients receiving vancomycin was 25% higher (RR=1.25, 95% CI=1.18-1.31) compared to those not receiving vancomycin. The expected hospital LOS in days among patients admitted to the ICU was 65% higher (RR=1.65, 95% CI=1.57-1.75) compared to those not admitted to the ICU prior to matching. For every 10-year increase in age, the expected hospital LOS in days increased by 3% (RR=1.03, 95% CI=1.02-1.05). After matching, patients who received vancomycin have a significantly longer hospital LOS compared those who did not receive the drug (Table 1, median=7

vs 6 days,  $P=0.002$ ). Specifically, the expected hospital LOS in days among patients receiving vancomycin was 23% higher (RR=1.23, 95% CI=1.15-1.30) compared to those not receiving vancomycin after matching on baseline characteristics.

### De-escalation Comparison

Of the 294 patients that received vancomycin, 44 were excluded from this analysis, with 18 being due to having a hospital LOS  $\leq 3$  days, 10 for having died  $\leq 3$  days from the date of admission, and 16 were excluded for having a positive MRSA finding (10 positive sputum cultures, 5 positive blood cultures, and 1 positive MRSA nasal PCR) leaving a total of 250 patients before matching. Baseline characteristics of the de-escalation groups before and after matching are listed in Table 3. Prior to matching, patients who were de-escalated from vancomycin were significantly older (Mean=69.9 vs 64.7 years,  $P=0.012$ ), and less likely to be admitted to the ICU (25% vs 43%,  $P=0.002$ ) compared to those who were not de-escalated.

Propensity score matching resulted in a matched sample of 192 patients (96 in each group). In the matched samples, all ASMDs were below 0.20, indicating patients who were de-escalated and those who were not de-escalated were well-matched on all baseline characteristics. No statistically significant differences in baseline characteristics were found after matching (Table 2). Prior to matching, there were no statistically significant differences in mortality between the de-escalation groups (log-rank  $P=0.90$ ). Similar results were found after matching, as no significant differences were found in mortality between the two groups (Figure 2, log-rank  $P=0.86$ ).

Prior to matching, median hospital LOS among non-de-escalated patients was 9 days (IQR=6, 14) compared to 7 days (IQR=5, 10) in those who were de-escalated (Table 2,  $P=0.001$ ). Results from a backwards selection Poisson regression model

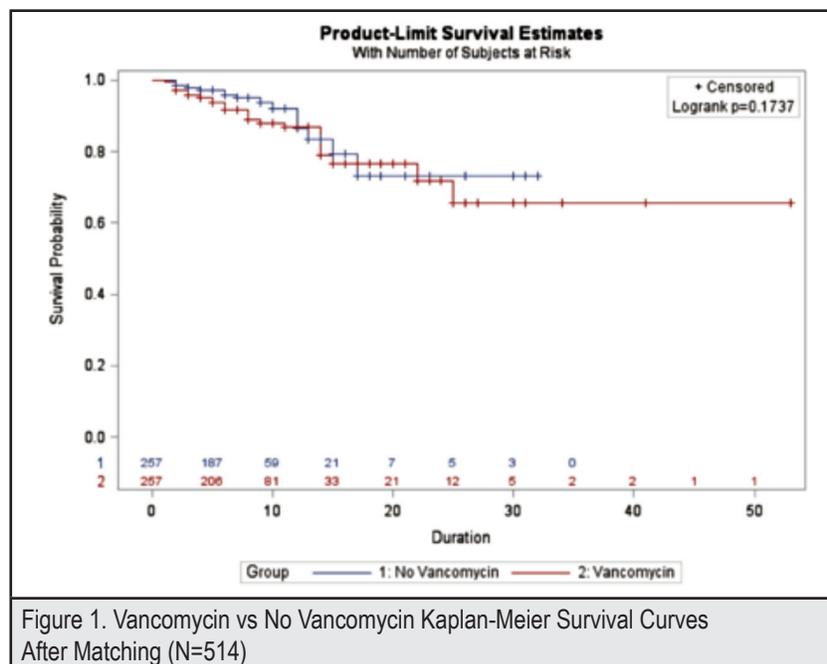


Figure 1. Vancomycin vs No Vancomycin Kaplan-Meier Survival Curves After Matching (N=514)

demonstrated that patients' hospital LOS was significantly associated with the de-escalation group ( $P < .001$ ), diabetes ( $P = .008$ ), sepsis ( $P = .002$ ), and ICU admission ( $P < .001$ ) in the unmatched sample. Specifically, the expected hospital LOS in days among non-de-escalated patients was 27% higher (RR = 1.27, 95% CI = 1.17-1.38) compared to those de-escalated. After matching, patients who were not de-escalated contin-

ued to have a significantly longer hospital LOS compared to those who were de-escalated (Table 2, median = 8 vs 7 days,  $P = .005$ ). Specifically, the expected hospital LOS in days among non-de-escalated patients was 36% higher (RR = 1.36, 95% CI = 1.25 - 1.50) compared to those de-escalated after matching on baseline characteristics.

Variable	Unmatched Sample (N=250)			Matched Sample (N=192)		
	Not De-escalated (n=141)	De-escalated (n=109)	P value	Not De-escalated (n=96)	De-escalated (n=96)	P value
<b>Baseline Characteristics</b>						
Age (years), mean (SD) median (IQR)	64.7 (16.6) 66 (56, 76)	69.9 (16.0) 68 (61, 83)	.012*	69.3 (14.7) 70.5 (60, 80)	69.5 (16.2) 68 (60, 83)	.92
Male, n (%)	79 (56%)	58 (53%)	.66	51 (53%)	52 (54%)	.88
Diabetes, n (%)	50 (35%)	39 (36%)	.96	37 (39%)	32 (33%)	.45
COPD, n (%)	35 (25%)	27 (25%)	.99	27 (28%)	23 (24%)	.51
Immunocompromised, n (%)	17 (12%)	7 (6%)	.134	8 (8%)	7 (7%)	.79
Renal disease, n (%)	40 (28%)	38 (35%)	.27	30 (31%)	31 (32%)	.88
Sepsis, n (%)	73 (52%)	46 (42%)	.133	44 (46%)	41 (43%)	.66
Prior antibiotics within 90 days, n (%)	50 (35%)	36 (33%)	.69	31 (32%)	32 (33%)	.88
ICU admission, n (%)	61 (43%)	27 (25%)	.002*	31 (32%)	27 (28%)	.53
Antibiotic therapy treatment duration** (days), mean (SD) median (IQR)	9.6 (5.9) 8 (5, 12)	6.9 (4.0) 6 (4, 8)	<.001*	9.2 (5.6) 8 (5, 11)	6.8 (3.8) 6 (4, 9)	.001*
Number of antibiotics**, mean (SD) median (IQR)	3.2 (1.4) 3 (2, 4)	2.7 (1.2) 3 (2, 3)	.025	3.0 (1.3) 3 (2, 4)	2.8 (1.2) 3 (2, 3.5)	.24
<b>Primary Outcomes</b>						
Mortality, n (%)	21 (15%)	9 (8%)	.109	13 (14%)	6 (6%)	.091
Hospital length of stay (days), mean (SD) median (IQR)	11.6 (8.3) 9 (6, 14)	8.3 (4.5) 7 (5, 10)	.001*	11.3 (8.4) 8 (6, 13.5)	8.3 (4.4) 7 (5, 10)	.005*

\* $P < .025$ ; \*\*Not included as a matching variable in propensity score modeling.

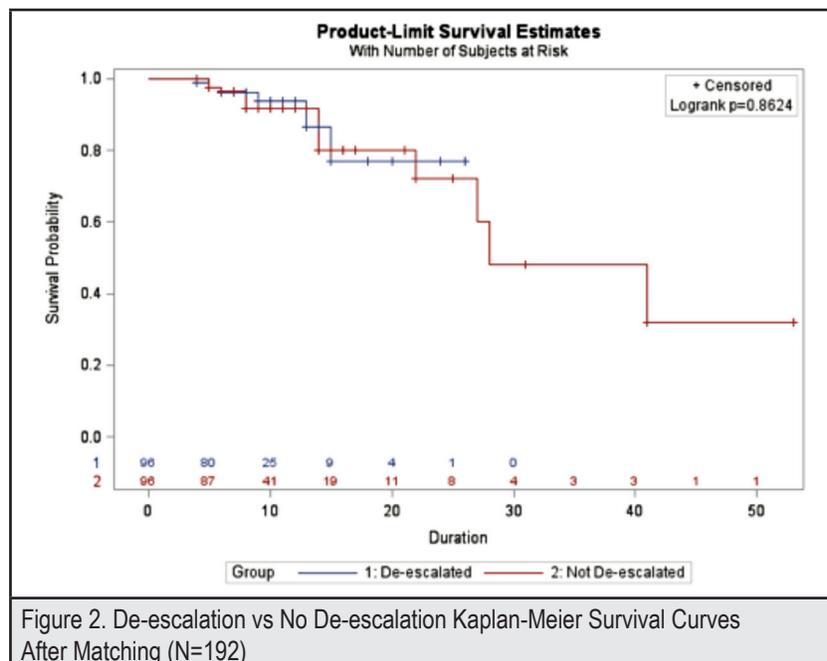


Figure 2. De-escalation vs No De-escalation Kaplan-Meier Survival Curves After Matching (N=192)

## Discussion

Based on IDSA pneumonia treatment guidelines, MRSA coverage is recommended in those with a high risk for mortality or if MRSA prevalence is 20% or greater.<sup>3,4</sup> Based upon these guidelines, Hawaii's reported 2015 MRSA prevalence was 38.2%, which would suggest the use of empiric vancomycin in Hawaii's pneumonia patient population.<sup>3,4,9</sup> However, our findings show that while 294 (38.3%) of our patients received vancomycin, only 20 (2.6%) patients had a positive MRSA finding and 274 (35.7%) patients had no evidence of MRSA infection or colonization. This study demonstrates two points: (1) the low prevalence of MRSA pneumonia within the HPH system, as well as (2) the overuse of vancomycin for treating pneumonia. Overuse of antibiotics not only puts patients at risk for adverse drug reactions but also provides opportunities for antibiotic resistance. Avoiding the use of unnecessary initial antibiotics or prompt de-escalation are potential solutions to antibiotic overuse.

Prior to matching, there was a significant difference in mortality between the two groups in the vancomycin comparison with the vancomycin group having a higher mortality rate. However, due to the significant differences in certain baseline characteristics, such as ICU admission and sepsis, potential confounders were likely, and the causality of mortality was uncertain. It was unclear whether the vancomycin was increasing the mortality rate or if the patients were already at an increased risk for mortality and why they then received vancomycin. To address this, a propensity score matching was done. After matching, there were statistically significant differences in mortality, as shown in Table 1. However, it was concluded there were no significant differences in mortality using the Kaplan-Meier methods (Figure 1), as we were interested in analyzing mortality as a time-to-event variable and the most appropriate methodology would rely on survival methods given their ability to account for censoring that the methods in Table 1 do not properly account for. In the de-escalation comparison, there were no significant differences in mortality before and after matching. LOS was significantly longer in both the vancomycin and de-escalation comparisons before and after matching.

A longer LOS contributes to an increase in healthcare costs and increases the risk for hospital-acquired infections, which could result in worse outcomes. Since our data demonstrates that LOS is increased with the use of vancomycin, decreasing use of the drug or utilizing prompt de-escalation would decrease

LOS. The significant differences in LOS for both comparisons before and after matching supports this option. Lowering LOS would parallel both lower patient costs and the risk of hospital acquired infections, and prevent negative outcomes. Even though there were no significant differences in mortality in both comparisons, vancomycin use did not improve or worsen outcomes. Drug therapy intervention via antimicrobial stewardship intervention will help to reduce the growing challenge of antibiotic resistance.

One study limitation is that the study did not distinguish between CAP versus HAP. Both CAP and HAP are treated differently and have different prevalence rates of MRSA, with HAP having a higher MRSA prevalence rate. Another limitation was the relatively small sample size for the de-escalation comparison. After matching, there was a change towards significance for mortality (Table 2). This could have been due to insufficient power in the de-escalation comparison.

## Conclusion

Overall, in our retrospective review, only 2.6% of the population had positive MRSA findings while 38.3% received vancomycin suggesting vancomycin overuse. No difference in mortality was found in both comparisons showing no negative outcomes associated with not using vancomycin. Not using vancomycin and de-escalating off of vancomycin showed potential benefits in lowering LOS. This could reduce hospital costs and the unnecessary risk for hospital-acquired infections, which could reduce negative outcomes. Before any strong recommendations can be made, further prospective studies with larger numbers of patients are needed to confirm the findings. However, no difference in mortality, a lower LOS, and a low MRSA prevalence rate support an appropriate recommendation to limit vancomycin use in pneumonia as clinically appropriate. Should clinical signs and symptoms suggest empiric prescribing of vancomycin, a MRSA nasal PCR should be ordered with cultures to guide rapid de-escalation in cases of negative PCRs.

## Disclosure Statement/Conflict of Interest

None of the authors identify any disclosures or conflicts of interest.

### Authors' Affiliations:

- The Daniel K. Inouye College of Pharmacy, University of Hawai'i at Hilo, Hilo, HI (ASY, BTF, ALH, AJL, RAG)
- Hawai'i Pacific Health, Honolulu, HI (ASY, BTF, RAG)

## References

1. Antibiotic resistance threats in the United States, 2013. Centers for Disease Control and Prevention Web Site. <https://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf>. Accessed February 20, 2017.
2. Strategies to assess antibiotic use to drive improvements in hospitals. Centers for Disease Control and Prevention Web Site. <https://www.cdc.gov/antibiotic-use/healthcare/pdfs/strategies-to-assess-antibiotic-use-in-hospitals-508.pdf>. Accessed February 20, 2017.
3. Kalil AC, Metersky ML, Klompas M, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis*. Published July 14, 2016.
4. Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis*. 2007; 44 Suppl 2:S27.
5. Rubinstein E, Kollef MH, Nathwani D. Pneumonia Caused by Methicillin-Resistant *Staphylococcus aureus*. *Clinical Infectious Diseases*. 2008;46:S378-85.
6. Minejima E, Lou M, Nieberg P, et al. Patients presenting to the hospital with MRSA pneumonia: differentiating characteristics and outcomes with empiric treatment. *BMC Infectious Diseases*. 2014;14:252.
7. Jacobs DM, Shaver A. Prevalence of and outcomes *Staphylococcus aureus* pneumonia among hospitalized patients in the United States, 2009-2012. *American Journal of Infection Control*. 2017;45:404-9.
8. Self WH, Wunderink RG, Williams DJ, et al. *Staphylococcus aureus* Community-acquired Pneumonia: Prevalence, Clinical Characteristics, and Outcomes. *Clinical Infectious Diseases*. 2016;63(3):300-9.
9. 2015 Hawaii Statewide Antibiogram for Selected Bacteria of Public Health Significance. Hawaii State Department of Health Web Site. [https://health.hawaii.gov/docd/files/2017/01/2015\\_Hawaii\\_Statewide\\_Antibiogram\\_Final.pdf](https://health.hawaii.gov/docd/files/2017/01/2015_Hawaii_Statewide_Antibiogram_Final.pdf). Accessed May 1, 2018.
10. Schlueter M, James C, Dominguez A, Tsu L, Seymann G. Practice patterns for antibiotic de-escalation in culture-negative healthcare-associated pneumonia. *Infection*. 2010;38(5):357-362.
11. McDanel JS, Perencevich EN, Diekema DJ, et al. Comparative effectiveness of beta-lactams versus vancomycin for treatment of methicillin-susceptible *Staphylococcus aureus* bloodstream infections among 122 hospitals. *Clin Infect Dis*. 2015;61(3):361-7.
12. Schweizer ML, Furuno JP, Harris AD, et al. Comparative effectiveness of nafcillin or cefazolin versus vancomycin in methicillin-susceptible *Staphylococcus aureus* bacteremia. *BMC Infectious Diseases*. 2011;11:279.
13. Wong D, Wong T, Romney M, Leung V. Comparative effectiveness of  $\beta$ -lactam versus vancomycin empiric therapy in patients with methicillin-susceptible *Staphylococcus aureus* (MSSA) bacteremia. *Annals of Clinical Microbiology and Antimicrobials*. 2016;15:27.
14. Baby N, Faust AC, Smith T, Sheperd LA, Knoll L, Goodman EL. Nasal Methicillin-Resistant *Staphylococcus aureus* (MRSA) PCR Testing Reduces the Duration of MRSA-Targeted Therapy in Patients with Suspected MRSA Pneumonia. *Antimicrobial Agents and Chemotherapy*. 2017;61(4):e02432-16.
15. Dangerfield B, Chung A, Webb B, Seville MT. Predictive Value of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Nasal Swab PCR Assay for MRSA Pneumonia. *Antimicrobial Agents and Chemotherapy*. 2013;58(2):859-864.
16. Cohen, J. (1988). *Statistical power analysis for the behavioral sciences*. Hillsdale: Lawrence Erlbaum Associates.
17. Wright SP. (1992, December). Adjusted p-values for simultaneous inference. *Biometrics*. 48:1005-13. doi:10.2307/2532694
18. Ho DE, Imai K, King G, Stuart E. (2011). MatchIt: Nonparametric preprocessing for parametric causal inference. *J Stat Softw*. 42:1-28.
19. Little RJ, Rubin DB. 1987. *Single imputation methods*. In Roderick J. A. Little and Donald B. Rubin (Eds). *Statistical analysis with missing data*. pp. 59-74. New York, NY: John Wiley and Sons.